11.6 min (28.7%, **5b**). In three of the aliquots (1 min, 15 min, 1 h), a small peak (<1%) was detectable at 9.3 min, corresponding in retention time to *cis*-vinylsilane **6a**; in the other two aliquots, no peak was detectable at 9.3 min.

A separate reaction without the internal standard gave similar results.

Acknowledgment. We gratefully acknowledge the National Science Foundation (Grants CHE-83-04867 and CHE-86-07561) for support of this work. We thank Dr. Carlyle Storm for assistance with the low-temperature 200-MHz NMR experiment. High-resolution mass spectral determinations were performed at the Midwest Center for Mass Spectrometry, an NSF Regional Instrumentation Facility.

Notes

Fluoromalonaldehyde Bis(dialkyl acetals): Synthesis by Carbene Condensation and Transformation to Dialkyl Fluoromalonates and Fluorinated Heterocyclic Compounds

Huguette Molines and Claude Wakselman*

CNRS-CERCOA, 2, rue Henry Dunant, 94320 Thiais, France

Received March 16, 1989

Fluoromalonaldehyde (**1**) has been used as a fluorinating building block for synthesis of various fluorine-substituted carbocyclic and heterocyclic compounds.[1] To date, only one preparation of **1** has been reported.[2] This useful reagent was prepared by Vilsmeier formylation of sodium fluoroacetate followed by alkaline hydrolysis of the 2-fluoro-3-(dimethylamino)acrolein so obtained. The toxicity of the starting material and the poor overall yield (15%) limited the interest for this fluorinating building block.

OCH-CHF-CHO

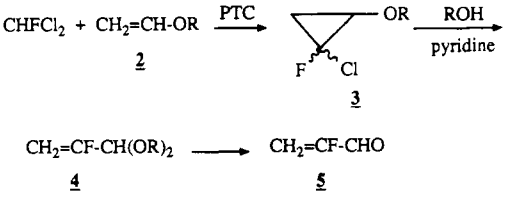
1

We report here an easy two-step synthesis of acetals of fluoromalonaldehyde starting from dichlorofluoromethane and dioxene. Then we will show how these new compounds can be used as starting material in place of **1** to get fluorinated heterocyclic compounds and for a new and convenient way to dialkyl fluoromalonates.[3]

Some years ago we developed a carbene process for the synthesis of 2-fluoroacrolein (**5**).[4] Chlorofluorocarbene generated from dichlorofluoromethane was condensed on enol ether **2**. Phase-transfer catalysis (PTC) was used, and these mild conditions permitted isolation of the dihalocyclopropane **3**.[4,5] The following step for the synthesis of 2-fluoroacrolein (**5**) was the conversion of **3** to the acetal **4** by refluxing it in pyridine and alcohol (Scheme I).

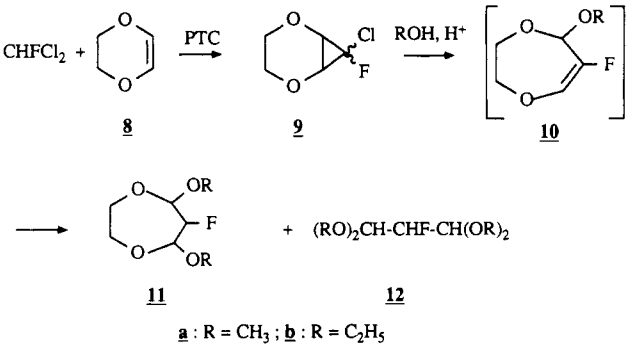
The application of this method to 1,2-dialkoxyethylene **6** should lead in two steps to the acetal **7**, a masked form of fluoromalonaldehyde. Reagent **6** ought to be readily available to make this synthetic pathway attractive. Among compounds of type **6**, only 2,3-dihydro-*p*-dioxin

Scheme I



2 **3** **4** **5**

Scheme II



8 **9** **10** **11** **12**

a: R = CH_3; **b**: R = C_2H_5

(dioxene) (**8**) could be easily prepared on a large scale from diethylene glycol.[6]

RO-CH=CH-OR RO-CH=CF-CH(OR)$_2$

6 **7**

Results and Discussion

Carbene Condensation. Condensation of dioxene (**8**) with chlorofluorocarbene under phase-transfer conditions led to 7-chloro-7-fluoro-2,5-dioxabicyclo[4.1.0]heptane (**9**) (Scheme II). Liquid–liquid PTC (50% aqueous sodium hydroxide–dichloromethane–benzyltriethylammonium chloride) at 5–10 °C gave **9** in 91% isolated yield. A mixture of cis (**9c**) and trans (**9t**) isomers was obtained in the ratio 58/42. These configurations were determined on the basis of the ^{19}F NMR chemical shifts and coupling constants in **9c** (δ = −145 ppm, J_{HF} = 14 Hz) and in **9t** (δ = −170 ppm, J_{HF} = 0 Hz).[7,8]

A much simpler solid–liquid PTC procedure[9] using tris(3,6-dioxaheptyl)amine (TDA-1)[10] was also tried, giving

(1) Reichardt, C.; Halbritter, K. *Justus Liebigs Ann. Chem.* **1975**, 470.
(2) Reichardt, C.; Halbritter, K. *Justus Liebigs Ann. Chem.* **1970**, *737*, 99.
(3) Presented at the 12th International Symposium on Fluorine Chemistry, Santa Cruz, CA, Aug 1988.
(4) Molines, H.; Nguyen, T.; Wakselman, C. *Synthesis* **1985**, 754 and references cited therein.
(5) This carbene process was also applied to 1,1-dialkoxyethylene. Nguyen, T.; Molines, H.; Wakselman, C. *Synth. Commun.* **1985**, *15*, 925.
(6) Moss, R. D.; Paige, J. *J. Chem. Eng. Data* **1967**, *12*, 452.
(7) Camps, F.; Coll, J.; Fabbrias, G.; Guerrero, A. *J. Fluorine Chem.* **1985**, *29*, 261.
(8) Emsley, J. W.; Phillips, L.; Wray, V. *Fluorine Coupling Constants*; Pergamon Press: New York, 1977; p 209.
(9) The workup was only a filtration.
(10) Soula, G. *J. Org. Chem.* **1985**, *50*, 3717.

0022-3263/89/1954-5618$01.50/0

unfortunately a lower yield (36%).

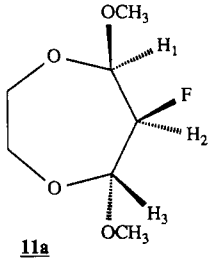
Transformation of the Adduct 9. The thermal decomposition of the adduct **9** was performed in refluxing alcohol with acidic catalysis[11] and gave a mixture of two acetals, **11** and **12** (Scheme II). The cyclic acetal **11** was due to the addition of alcohol to the expected intermediate **10** whereas the bis(dialkyl acetal) **12** was formed by subsequent transacetalation of **11**. The ratio of the two acetals (**12**/**11**) was determined by the ^{19}F NMR analysis[12] and was 75/25 when methanol was used and 65/35 in the case of ethanol.

This transformation needed several days to reach completion. For instance, **9** had to be refluxed for 1 week in absolute ethanol with a few drops of concentrated sulfuric acid to give a mixture of acetals **11b** and **12b** in 80% yield (after distillation).[13] The same experiment carried out at 120 °C in an autoclave gave complete transformation after 7 h, but the yield was only 48%, with a significant residue remaining after the distillation.

Separation of the two acetals **11** and **12** proved difficult, and it was achieved successfully only when R was methyl by using an efficient distillation apparatus (microdistillation Fischer-Spaltrohr apparatus), but further condensations of the acetals would show that the mixture could be directly used. When R was ethyl, complete identification was achieved by comparison of the ^{13}C NMR spectrum of the mixture of acetals **11b** and **12b** with those of **11a** and **12a**.[14]

We have confirmed that refluxing **11a** with methanol and sulfuric acid gave **12a**. We never succeeded in getting only **12** even after refluxing the mixture for 2 weeks; **11** always remained.

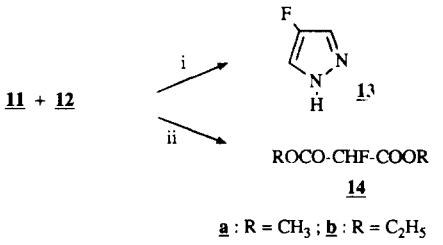
The stereochemistry of the cyclic acetal **11a** was assigned by spectral analysis of the values of the ^1H (300 MHz) and ^{19}F (56.4 MHz) NMR coupling constants: J_{FH1} = 19 Hz, J_{FH3} = 7 Hz, J_{H1H2} = 2 Hz, and J_{H2H3} = 7 Hz. With these values, the fluorine atom must be in a cis situation with respect to a methoxy group and trans to the other one.[8]



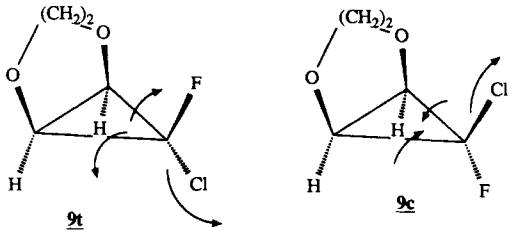
11a

We also followed the reaction progress by ^{19}F NMR analysis, and we observed that the long time required for complete transformation of **9** was due to the trans (or exo) isomer **9t** and that the cis (or endo) isomer **9c** had completely disappeared after refluxing for 2 or 3 h. This experimental observation was in accordance with the Woodward–Hoffmann selection rules.[15] The solvolysis had to proceed with concerted disrotatory ring opening. The solvolysis of **9t** would induce the formation of a trans double bond in the ring, which is disfavored. **9t** should undergo ring expansion much more slowly than **9c**.[16]

Scheme III[a]



[a] (i) H_2NNH_2, 2HCl, EtOH–H_2O, reflux; (ii) Caro acid, ROH.



Transformation to 4-Fluoropyrazole. The mixture of acetals **11** and **12** could be directly used for the synthesis of fluorinated heterocyclic compounds. For example, condensation of a mixture of **11b** and **12b** with hydrazine dihydrochloride in aqueous ethanol at reflux gave 4-fluoropyrazole (**13**) in 80% yield (Scheme III).

Oxidation to Dialkyl Fluoromalonates. Straightforward oxidation of acetals of fluoromalonaldehyde appeared to be a convenient synthesis of dialkyl fluoromalonates.[17] It was performed with Caro acid[18] in alcohol at room temperature (Scheme III). A mixture of **11b** and **12b** in ethanol gave diethyl fluoromalonate (**14b**) in 54% isolated yield. **14b** was also prepared in 43% yield directly from the solvolysis mixture without isolating acetals. Thus diethyl fluoromalonate was obtained in a two-step synthesis with a 39% overall yield from dioxene.

Experimental Section

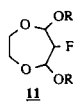
General Methods. ^1H and ^{19}F NMR spectra, unless otherwise specified, were recorded respectively at 60 and 56.45 MHz with a Varian EM 360 L NMR spectrometer equipped with a proton/fluorine probe. Higher field NMR spectra were recorded at 300 MHz (^1H) and 75.43 MHz (^{13}C) on a Brüker AM-300 apparatus. ^1H and ^{13}C NMR chemical shifts are reported in parts per

(11) Acidic conditions were used instead of basic conditions as previously described.[4] Indeed, refluxing **9** with pyridine and alcohol led to a mixture consisting of **10**–**12** and nonidentified compounds.

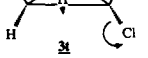
(12) The ^{19}F NMR chemical shift in **12** was lower than in **11**; for example, in **11a**, δ = −213 ppm, and in **12a**, δ = −211 ppm.

(13) The yield was calculated as if the product were only **12b** (molecular weight: **12b** = 238; **11b** = 208).

(14) ^{13}C NMR chemical shifts in parts per million (75.43 MHz) of **11** and **12** are as follows. **11a**: C_2 and C_4, 103.9 (dd), 104.5 (dd); C_3, 92.7 (ddd); C_6 and C_7, 68.3 (t), 68.4 (t). **11b**: C_2 and C_4, 102.9 (dd), 103.95 (dd); C_3, 93.25 (ddd); C_6 and C_7, 68.2 (t), 68.35 (t). **12a**: C_1 and C_3, 104.3 (dd); C_2, 93.1 (dd). **12b**: C_1 and C_3, 102.46 (dd), C_2, 93.9 (dd).



11



12

a : R = CH_3 ; b : R = C_2H_5

(15) (a) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim, 1970. (b) Depuy, C. H.; Schnack, L. G.; Hausser, J. W. *J. Am. Chem. Soc.* **1966**, *88*, 3343. (c) Parham, W. E.; Parham, F. M.; Dooley, J. F.; Meilahn, M. K. *J. Org. Chem.* **1968**, *33*, 3651.

(16) The contrary was observed in the solvolysis of the dihalocyclopropane **3**. The trans isomer **3t** was completely opened while the cis isomer **3c** remained unchanged.[4] In that case the best way for the concerted ring opening was this, in which the alkoxy group trans to the leaving group rotated outward:[15c]

3t

(17) For the other synthesis of dialkyl fluoromalonates, see: Ishikawa, N.; Takaoka, A *Chem. Lett.* **1981**, 107.

(18) Nishihara, A.; Kubota, I. *J. Org. Chem.* **1968**, *33*, 2525.

million (ppm) downfield relative to tetramethylsilane. ^{19}F NMR chemical shifts are given in parts per million downfield relative to trichlorofluoromethane. IR spectra were recorded on a Perkin-Elmer 1420 spectrometer and are expressed in cm^{-1}. Elemental analyses were performed by the Service de Microanalyse, Université Pierre et Marie Curie, Paris. Mass spectra were determined on a Nermag R30-10 instrument by Professor J. C. Tabet, Université Pierre et Marie Curie, Paris. Ether was diethyl ether. Dichlorofluoromethane (Freon-21) was a generous gift from Atochem and tris(3,6-dioxaheptyl)amine (TDA-1) from Rhône-Poulenc.

7-Chloro-7-fluoro-2,5-dioxabicyclo[4.1.0]heptane (9). Liquid–Liquid PTC. Dichlorofluoromethane (23.2 g, 0.225 mol) was bubbled into a vigorously stirred mixture of dioxene (8; 12.9 g, 0.15 mol), dichloromethane (15 mL), benzyltriethylammonium chloride (0.05 g), and aqueous sodium hydroxide (50% by wt, 45 mL) at 5–10 °C. Stirring at 20 °C was continued for 14 h. Then water (300 mL) was added, and the organic products were extracted with dichloromethane (3 × 200 mL). The extract was washed with brine (100 mL) and dried over sodium sulfate. The solvent was evaporated under vacuum (20 mmHg), and the residue was distilled to give **9** (20.8 g, 0.1365 mol; 91%) as a mixture of two isomers **9c** (cis, 58%) and **9t** (trans, 42%): bp 67–68 °C (20 mmHg); ^1H NMR ($CDCl_3$) 3.6–4.1 (mult); ^{19}F NMR ($CDCl_3$) –145 (cis isomer, t, $^3J_{HF}$ = 14 Hz), –170 (trans isomer, s). Anal. Calcd for $C_5H_6ClFO_2$ (152.55): C, 39.36; H, 3.96. Found: C, 39.76; H, 3.42.

Solid–Liquid PTC. Dichlorofluoromethane (15.45 g, 0.15 mol) was bubbled into a vigorously stirred mixture of dioxene (8.6 g, 0.1 mol), dichloromethane (50 mL), TDA-1 (1.6 g, 5 mmol), and sodium hydroxide reduced to powder (10 g, 0.25 mol) at 5–10 °C. The mixture was stirred for 14 h at 20 °C and then filtered. The solid was washed with dichloromethane (3 × 30 mL), the organic solution was evaporated under vacuum (20 mmHg), and the residue was distilled to give **9** (5.49 g, 0.031 mol; 36%).

Fluoromalonaldehyde Bis(dimethyl acetal) (12a) and 3-Fluoro-2,4-dimethoxy-1,5-dioxacycloheptane (11a). A mixture of **9** (8.05 g, 0.053 mol), methanol (53 mL), and concentrated sulfuric acid (0.35 mL) was refluxed for 8 days. The conversion (verified by ^{19}F NMR) was 86%; 14% of **9t** was still remaining. Water (50 mL) was added. The products were extracted with ether (3 × 50 mL). The organic solution was neutralized with saturated aqueous sodium hydrogen carbonate, then washed with brine (2 × 20 mL), and dried over sodium sulfate. The solvents were evaporated under vacuum (20 mmHg), and the residue was distilled to give a mixture of **11a** (25%) and **12a** (75%) (6.1 g, 63%): bp 88–95 °C (20 mmHg). A second distillation was perfomed in a micro distillation Fischer-Spaltrohr apparatus giving **12a** (4.9 g, 0.027 mol; 51%) and **11a** (0.6 g, 3.3 mmol; 6%). **12a**: bp 87–89 °C (20 mmHg); ^1H NMR ($CDCl_3$, 300 MHz) 3.43–3.44 (2 s, 12 H), 4.3 (t, $^3J_{HH}$ = 4.6 Hz) and 4.44–4.5 (mult) (3 H); ^{19}F NMR ($CDCl_3$) –211 (dt, $^2J_{HF}$ = 47 Hz, $^3J_{HF}$ = 11 Hz); ^{13}C NMR ($CDCl_3$, 75.43 MHz) 57.5 (q), 57.9 (q), 93.1 (dd), 104.3 (dd), 104.4 (d). Anal. Calcd for $C_7H_{15}FO_4$ (182.19): C, 46.15; H, 8.3. Found: C, 46.31; H, 8.4. **11a**: bp 106–110 °C (20 mmHg); ^1H NMR ($CDCl_3$, 300 MHz) 3.45 (mult, 6 H), 3.96 (d mult, 4 H), 4.36 (ddd, 1 H, $^2J_{HF}$ = 47 Hz, $^3J_{HH}$ = 6.5 Hz and 2 Hz), 4.52 (t, 1 H, $^3J_{HF}$ = $^3J_{HH}$ = 6.5 Hz), 5.14 (dd, 1 H, $^3J_{HF}$ = 18 Hz, $^3J_{HH}$ = 2 Hz); ^{19}F NMR ($CDCl_3$) –213 (ddd, $^2J_{HF}$ = 47 Hz, $^3J_{HF}$ = 18 Hz and 6.5 Hz); ^{13}C NMR ($CDCl_3$, 75.43 MHz) 56,8 (q), 58.1 (q), 68.3 (t), 68.4 (t), 92.7 (ddd), 103.9 (dd), 104.5 (dd). Anal. Calcd for $C_7H_{13}FO_4$ (180.17): C, 46.66; H, 7.27. Found: C, 46.25; H, 8.16.

Fluoromalonaldehyde Bis(diethyl acetal) (12b) and 3-Fluoro-2,4-diethoxy-1,5-dioxacycloheptane (11b). The same procedure as for the preparation of **12a** and **11a** was followed starting from 6.1 g (0.04 mol) of **9**. After refluxing for 7 days, no more starting material was detected by ^{19}F NMR. The refluxing was stopped. The workup was the same. Distillation afforded a mixture of **11b** (35%) and **12b** (65%) (7.6 g; 80% calculated as if all were **12b**[13]): bp 118–122 °C (12 mmHg); ^1H NMR ($CDCl_3$, 300 MHz) 1.17 (mult), 3.46–3.7 (mult), 3.91 (d mult, 8 lines, OCH_2CH_2O **11b**), 4.25 and 4.3 (2 dt, CHF **11b** and **12b**, $^2J_{HF}$ = 47 Hz, $^3J_{HH}$ = 4.5 Hz), 4.54–4.6 (d mult), 5.1 (dd, CH **11b**, $^3J_{HH}$ = 1.5 Hz, $^3J_{HF}$ = 18.5 Hz); ^{19}F NMR ($CDCl_3$) –211 (dt, $^2J_{HF}$ = 47 Hz, $^3J_{HF}$ = 12 Hz), –213 (ddd, $^2J_{HF}$ = 47 Hz, $^3J_{HF}$ = 7 and 18 Hz); ^{13}C NMR ($CDCl_3$, 75.43 MHz) 17.76 (q), 17.84 (q), 17.91 (q), 65.4 (t, **11b**), 65.9 (t, **12b**), 66.3 (t, **11b**), 68.2 (t, **11b**), 68.35 (t, **11b**), 93.25 (ddd, **11b**), 93.9 (dd, **12b**), 102.46 (dd, **12b**), 102.9 (dd, **11b**), 103.95 (dd, **11b**); MS (chemical ionization, NH_3) 256 [MNH_4^+ (**12b**)], 239 [MH^+ (**12b**)], 226 [MNH_4^+ (**11b**)], 210 [MNH_4^+ (**12b**) – C_2H_5OH], 209 [MH^+ (**11b**)], 180 [MNH_4^+ (**11b**) – C_2H_5OH].

4-Fluoropyrazole (13). A mixture of **11b** and **12b** (2.38 g, 0.01 mol[13]), hydrazine dihydrochloride (1.05 g, 0.01 mol), water (1.5 mL), and ethanol (1 mL) was refluxed for 2 h. Then the mixture was cooled and water (4 mL) and sodium carbonate (2 g) were added. The mixture was filtered and the solid washed with ether (2 × 10 mL). After decantation, the aqueous solution was extracted with ether (2 × 10 mL). The organic solution was washed with brine (2 × 5 mL) and dried over sodium sulfate. The solvents were evaporated under vacuum (20 mmHg). A flash distillation of the residue under vacuum (18 mmHg) gave **13** (0.69 g, 8 mmol; 80%): bp 86–88 °C (18 mmHg) [lit.[1] bp 84 °C (15 mmHg)].

Diethyl Fluoromalonate (14b). To a vigorously stirred solution of **11b** and **12b** (7.14 g; 0.03 mol) in absolute ethanol (60 mL) at 5–10 °C was added the Caro acid[18] prepared from 90% sulfuric acid (42 g) and ammonium persulfate (34.2 g, 0.15 mol). After being stirred for 16 h at room temperature, the mixture was diluted with cold water (200 mL) and extracted with ether (3 × 150 mL). The organic solution was washed with brine (2 × 75 mL) and then dried over sodium sulfate. The solvents were evaporated under vacuum (20 mmHg), and the residue was distilled to give **14b** (2.9 g, 0.0163 mol; 54%): 94–96 °C (12 mmHg) [lit.[17] 110–111 °C (20 mmHg)].

Dimethyl Fluoromalonate (14a). The same procedure as for the preparation of **14b** was followed starting from **12a** (3.3 g, 0.018 mol) in solution in methanol (18 mL). The solvents were distilled at atmospheric pressure, and the residue was distilled to give **16a** (1.5 g, 0.01 mol; 55%): 82–85 °C (15 mmHg) [lit.[17] 111–112 °C (45 mmHg)].

Acknowledgment. This work was supported by Rhône-Poulenc, for which we are grateful. We thank Atochem for a generous gift of dichlorofluoromethane.

Registry No. **8**, 543-75-9; **9c**, 40623-36-7; **9t**, 40623-35-6; **11a**, 122875-58-5; **11b**, 122875-59-6; **12a**, 120131-06-8; **12b**, 120131-05-7; **13**, 35277-02-2; **14a**, 344-14-9; **14b**, 685-88-1; $CHFCl_2$, 75-43-4.

One-Pot Synthesis of β-Keto Sulfones and β-Keto Sulfoxides from Carboxylic Acids

C. Alvarez Ibarra,* R. Cuervo Rodríguez, M. C. Fernández Monreal, F. J. García Navarro, and J. Martín Tesorero

Departamento de Química Orgánica I, Facultad de C. Químicas, Universidad Complutense, Ciudad Universitaria, s/n 28040, Madrid, Spain

Received February 17, 1989

Many synthetic applications of β-oxo sulfones[1–8] and β-oxo sulfoxides[9–30] have been reported in the literature.

(1) (a) Koutek, B.; Pavlickova, L.; Soucek, M. *Collect. Czech. Chem. Commun.* **1974**, *39*, 192. (b) Julia, M.; Badet, P. *Bull. Soc. Chim. Fr.* **1975**, 1363. (c) Kondo, K.; Tunemoto, D. *Tetrahedron Lett.* **1975**, 1397. (d) Cooper, G. K.; Dolby, I. J. *Tetrahedron Lett.* **1976**, 4765. (e) Ono, N.; Tamura, R.; Kaji, A. *Synthesis* **1977**, 690. (f) Schank, K.; Schmitt, H. G. *Chem. Ber.* **1978**, *11*, 3497. (g) Böhme, K.; Clement, B. *Tetrahedron Lett.* **1979**, 1737. (h) Messinger, P. M.; Kusuma, K. *Synthesis* **1980**, 565. (i) Scholz, D. *Liebigs Ann. Chem.* **1983**, 98.

(2) (a) Bartlett, P. A.; Green III, F. R.; Rose, E. H. *J. Am. Chem. Soc.* **1978**, *100*, 4852. (b) Jurasek, A.; Polakovicova, D.; Kovac, J. *Collect. Czech. Chem. Commun.* **1981**, *46*, 3115. (c) Scholz, D. *Liebigs Ann. Chem.* **1984**, 264. (d) Mandai, T.; Yanagi, T.; Araki, K.; Morisaki, Y.; Kavada, M.; Bebernitz, G. E.; Maynard, S. C.; Spagnolo, C. J. *Tetrahedron Lett.* **1985**, 169. (f) Kuth, M. J.; O'Brien, M. J. *J. Org. Chem.* **1985**, *50*, 3846.

(3) (a) Corey, E. J.; Chaykowsky, M. *J. Am. Chem. Soc.* **1965**, *87*, 1345. (b) House, H. O.; Larson, J. R. *J. Org. Chem.* **1968**, *33*, 61. (c) Trost, B. M.; Arndt, H. C.; Strege, P. E.; Verben, T. R. *Tetrahedron Lett.* **1976**, 3477.

0022-3263/89/1954-5620$01.50/0